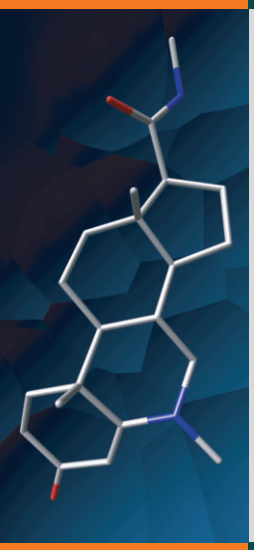


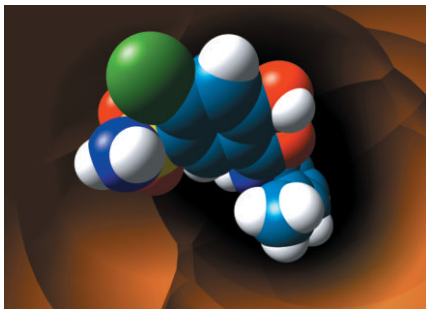
Strike

Powerful software for statistical modeling and QSAR

Strike is a highly capable statistical modeling package designed especially for chemists. An easy-to-use interface and wide variety of property prediction tools combine to make Strike the software of choice for developing structure-activity relationships.

SCHRÖDINGER.

The Advantages of QSAR and Statistical Modeling

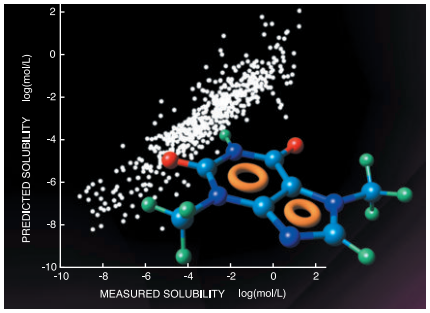


The aqueous solubility of a drug plays a key role in determining its pharmacokinetic profile. On the basis of structural descriptors and a calculated partition coefficient, Strike predicts the solubility of Xipamide to be 3.5 mol/L, which is in good agreement with the experimentally measured solubility of 3.8 mol/L.

The preparation of hit-rich virtual libraries can be a time consuming and challenging process. Incorrect characterization of drug-like properties will result in low HTS payoffs, with fewer, less promising hits. While scores of 2-D and 3-D descriptors can be rapidly calculated or predicted, these properties are of limited use unless they are correlated with drug action. Furthermore, in order to protect against over-fitting, any predictive relationship must use only a reasonable subset of descriptors with minimal covariance.

Quantitative structure-activity relationships (QSAR) and statistical modeling can be used to develop such predictive relationships, greatly improving the profile of virtual libraries. Chemically aware statistical modeling software combines sophisticated analysis tools with the ability to easily visualize the molecular structures and properties used to derive a structure-activity relationship. QSAR is the bedrock of rational drug design, and has repeatedly proven itself to be a low cost, high return investment.

Strike: Maximizing Returns in Drug Discovery

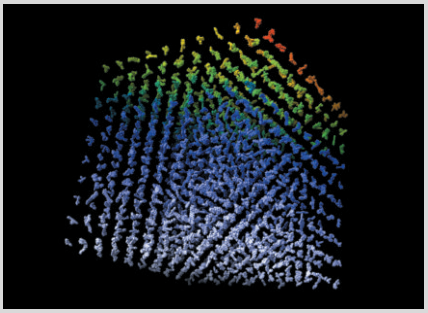


Strike is a chemically aware statistical modeling package that allows researchers to simultaneously visualize molecular structures and predictive relationships. A training set ligand is shown here alongside a scatter plot of predicted versus measured aqueous solubility.

Strike is Schrödinger's statistical modeling and QSAR package. Designed specifically with pharmaceutical and chemical researchers in mind, Strike features a broad variety of useful tools:

- **Versatile data management:** Strike takes advantage of Maestro's project management capabilities to import molecular properties and descriptors from spreadsheets, structure files, and other Schrödinger programs. The results of Strike predictions are automatically associated with structures and are easily manipulated using Maestro's project facility.
- **Validated QSAR:** Strike facilitates rapid hypothesis building and evaluation. Using a collection of chemical structures and associated properties, Strike applies one of several regression methods to derive a QSAR and return statistical measures of its accuracy and significance.
- **Prediction tools:** Once a satisfactory hypothesis has been obtained, Strike can quickly use this hypothesis to predict activities or drug-likeness of large virtual libraries.
- **Easy-to-use interface:** Strike is fully integrated within Maestro, Schrödinger's graphical user interface, for fast and convenient processing of a large number of compounds. The Maestro interface facilitates structure and data analysis, automation of repetitive tasks and visualization of results.
- **Cross-platform support:** Strike offers excellent performance on Linux and SGI.

Performance-Driven Technology

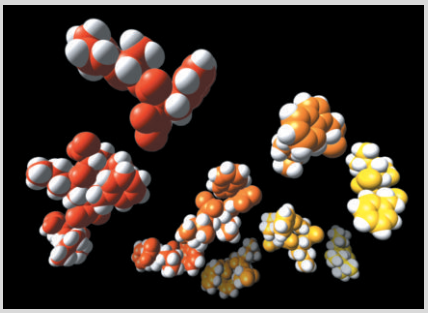


The adage "similar structure, similar activity" can be quantified by calculating the similarity of atom-pair connectivity between structures. A database of one thousand compounds has been ranked and the individual molecules colored and positioned in a three-dimensional box according to similarity with known thermolysin inhibitors – the most similar compounds are colored red, with decreasing similarity colored by orange, yellow, green, blue, and pale blue.

Strike allows researchers to derive accurate structure-activity relationships by providing them with an array of statistics tools packaged in a chemically aware interface:

- **Multiple regression methods:** Strike features multiple regression methods, including partial least squares (PLS), principal component analysis (PCA), and multiple linear regression (MLR). The interface allows for easy selection of input descriptors, and each method returns statistical measures of hypothesis quality automatically.
- **Accuracy and control:** Strike gives researchers control over regression method, training set, and input descriptors. Strike is also capable of automatically removing training set outliers, randomizing the training set, and selecting optimal regression parameters.
- **Univariate and bivariate statistical analysis:** Strike can characterize the properties of a structure library by performing univariate analysis, providing valuable insights when comparing databases. Bivariate statistics provide a measure of the model's accuracy, and allow researchers to protect against over-fitting and covariance among independent descriptors.
- **Similarity analysis:** Strike computes similarity between compounds using atom-pair connectivity and descriptor data.
- **Advanced visualization tools:** Because Strike was designed to offer fluid performance within the Maestro project facility, results are easily visualized. Plots are generated using associated structural data, providing insights into data clustering, descriptor diversity, hypothesis quality, and the accuracy of QSAR predictions.

Similarity Scoring



Strike calculates high similarity scores for the thermolysin inhibitors shown above, all of which are ranked in the top two percent of a virtual library that is routinely used in molecular docking experiments.

Before high-throughput screening, a rapid and effective way to characterize a compound library is to calculate the similarity scores between the database compounds and known actives. Computing the similarity score based on atom-pair connectivity between two structures is akin to comparing the 2-D structures, allowing researchers to identify promising molecular scaffolds within the database.

Strike's speed and predictive power are demonstrated by calculating the similarity scores for a one thousand compound database seeded with thermolysin inhibitors. After defining three inhibitors used to evaluate similarity, the entire database can be scored in less than fifteen seconds on a desktop computer. The full set of ten thermolysin inhibitors is accurately culled out among the top two percent of the Strike-ranked database.

Evaluation Copies

To request an evaluation copy of Strike, please contact info@schrodinger.com. Our staff of support scientists will be happy to assist you in giving Strike a thorough trial.

Strike

Powerful software for statistical modeling and QSAR

System Requirements:

LINUX
- Pentium or better
- Linux kernel 2.4 (Red Hat 7.3) or later
- 256 MB memory

SGI
- R5000 or better
- IRIX 6.5.2m or later
- 256 MB memory

Additional Information:

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info@schrodinger.com

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A Coordinated Family of Products

Strike is a powerful tool for statistical modeling and QSAR, and is an excellent complement to other Schrödinger software. Any energetic result or physicochemical property calculated by Schrödinger software can be easily incorporated as input for Strike's statistical models.

Strike is an ideal companion program for Schrödinger's **QikProp**, which rapidly calculates absorption, distribution, metabolism, and excretion (ADME) properties. QikProp can predict more than thirty-five pharmaceutically relevant 2-D and 3-D descriptors for several hundred thousand compounds per hour. Researchers wishing to characterize large virtual databases with Strike will find QikProp results to be ideal input descriptors.

All Schrödinger products are seamlessly integrated through the Maestro graphical interface.

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